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Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

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R C van Dijk

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NESTEC S.A.
Avenue Nestlé 55
1800 Vevey
SUISSE

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Nutritional composition against side effects of chemotherapy or radiotherapy

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Nutritional Composition against Side Effects of Chemotherapy or Radiotherapy

The present invention relates to a nutritional composition suitable to treat or alleviate side-effects of chemotherapy or radiotherapy, especially during cancer therapy. The invention also relates to a method for treating or preventing side effects of chemotherapy or radiotherapy.

The Background Art

Chemotherapy and/or radiotherapy are effective at destroying tumours because they target cells with high proliferation rates and hence fast growing tissues. Since stem cells of the gastrointestinal tract have high proliferation rates, too, a problematic side effect of chemotherapy or radiotherapy is the premature death of dividing epithelial cells.

In particular, chemotherapy and radiation therapy, which is often the treatment of choice for cancer patients, is associated with symptoms of intestinal impairment such as nausea, vomiting, diarrhoea, with or without blood in the stools (ulceration) and abdominal pain. These symptoms are linked to damages of the intestinal mucosa, the epithelial cell layer lining the intestines, which is in direct contact with the contents of the gastro-intestinal tract. During chemotherapy, the gastro-intestinal tract often contains anti cancer drugs, which may induce dietary intolerance and mucositis. Stomatitis is also frequently observed, and, together with diarrhoea, this strongly hampers the quality of life of the patient.

Several products on the market are communicated to be beneficial for cancer patients. For example PROSURE™, which is commercialised by Abbot Laboratories is a ready-to-drink (rtd) beverage with an energy density of about 1.27 kcal/ml, about 21% of energy being provided by protein. Furthermore, the product has 0.021 g fibre per ml. However, a nutritional composition, which is even higher in energy and provides more protein may prove to be advantageous over this product.

RESOURCE SUPPORT™, a rtd drink commercialised by Novartis, has about 1.52 kcal / ml and 23.3% energy provided by protein. This formula has 0.127 g

fibre per ml. It is an objective of the present invention to provide unique protein blends and a good taste adapted to cancer patients, while avoiding the presence of ingredients, which are present in amounts insufficient to be effective.

B van't Land et al, "Transforming Growth Factor-β2 protects the small intestine during methotrexate treatment in rats possibly by reducing stem cell cycling", British Journal of Cancer (2002) 87, 113-118, report that TGF-β2 isolated from bovine milk may reversibly arrest growth of epithelial stem cells during therapy. In a rat model, oral supplementation of rats exposed to methotrexate with TGF-β2 reduced the chemotherapy-associated weight loss.

WO 96/34614 discloses a method for preventing the damage that chemotherapy causes to the lining of the alimentary tract, by administering an effective amount of a milk product extract. This extract comprises GFE-2 (Growth Factor Extract), which is isolated from whey and nearly free of casein.

US 5,824,297 discloses the use of TGF-β3 for inhibiting cytotoxic poisoning due to anti-neoplastic therapy such as radiation treatment or chemotherapy. TGF-β3 is administered topically. US 5,824,297 does not disclose a nutritional composition.

A food composition including colostrum-derived growth factors is disclosed in WO 99/56758, whereby the composition is administered to prevent a disorder of the gut, for example, resulting from chemotherapy. However, colostrum can be obtained only during a short period of time after birth of the calf. Furthermore, WO 99/56758 does not disclose an embodiment of a nutritionally complete composition.

In view of the prior art, it is an objective of the present invention to provide a nutritional composition, which is suitable to provide macro-nutrients and micro-nutrient and which prevents and/or alleviates mucosal damage, in particular those resulting from radiation or chemotherapy.

that are chemically or radiation treated often have different taste preferences when compared to non- treated persons.

It is an objective of the present invention to provide nutrition and to prevent and/or treat side effects of chemotherapy or radiotherapy, for example with cancer patients.

Moreover, it is an objective to provide bio-active proteins derived or obtained from milk, which are able to remain active during passage through the gastro-intestinal tract.

It is an objective to provide a nutritional composition, comprising macro-nutrients, such as milk protein, which at the same time comprise bio-active proteins in effective quantities.

It is a further objective of the present invention to provide a nutritional supplement, for example a complete nutritional supplement.

Summary of the Invention

In a first aspect, the present invention provides a nutritional composition comprising a protein, a lipid and a carbohydrate source, which provides, in its liquid state, at least 1.3 kcal per ml, and which is characterised in that the protein source provides 20-30% of the energy of the composition and comprises milk protein containing bio-active proteins.

In another aspect, the present invention relates to a method for preventing, treating or alleviating side-effects during chemotherapy and/or radiation therapy comprising the step of administering the nutritional composition according to Claim 1.

Detailed Description of the Invention

Within the context of this specification the word "comprises" is taken to mean "includes, among other things". It is not intended to be construed as "consists of only".

The term "energy of the composition", as provided by a particular nutrient of the nutritional composition according to the present invention, is to be understood as "total energy of the composition", referring to the energy provided by all macro-nutrients together

The term TGF-β in an "active form" refers to TGF-β that has not irreversibly lost its ability to become biologically active. Hence, this term also refers to TGF-β, which is not active but may be activated by external conditions, in particular by passage through the gastro-intestinal tract. This may be evaluated in models that simulate the acidity of stomach or duodenum.

In the context of the present invention, the term "protein source" includes any amino-acid-based proteinogenic matter, such as intact or hydrolysed dietetic protein, as well as added peptides or free amino acids and mixtures of these, for example.

According to the invention, the milk protein comprises bioactive proteins.

In an embodiment, the nutritional composition according to the invention comprises whey or casein containing TGF-β, soluble CD14, Glucagon-like peptide 2, soluble Toll-2 receptor or a mixture containing several or all of these.

Soluble CD14 and its purification are disclosed in WO 00/22945, for soluble Toll-like receptor 2 (sTLR-2) see WO 03/025015. Generally, these bio-active proteins can be found, for example, in bovine milk, bovine colostrums, skimmed milk, whey fractions and specific casein fractions, but also in milk of other animal species such as goat, buffalo or sheep.

In a preferred embodiment of composition according to the present invention, the milk protein comprises 40-80% by weight of casein and 60-20% by weight of whey.

The casein may be provided in free form or in the form of a salt, for example, a sodium salt. It is also possible to provide the casein as a calcium or potassium-salt.

TGF-β is a particularly important bio-active protein. Therefore, in a preferred embodiment of the present invention, the milk protein comprises casein containing TGF-β, preferably TGF-β2. In the context of the present invention, the term TGF-β refers to active TGF–β, as opposed to denatured TGF-β, which is not biologically active.

Preferably, the TGF-β is naturally present in an active form in the milk protein. In other words, the preparation of the milk protein fractions used for the composition already contain TGF–β in sufficient amounts.

Preferably, the casein containing TGF-β2 may be produced in a "mild" or "protective" way, which preserves bio-active molecules in milk.

Casein containing bio-active molecules, such as TGF-β2, may be obtained by processes, wherein casein is precipitated by lowering the pH of milk with decationised whey and/or milk.

For example, FR 1 469 793 discloses a process for obtaining casein by precipitating casein by lowering the pH with decationised whey. This process serves for the concurrent production of whey for the manufacture of lactose and nutritional compositions for mast.

The process comprises, solely or in combination with each other, one, several or all of the following features:

- Decreasing the pH of skimmed milk by addition of whey, the pH of which has been decreased by exchange of cations;
- The whey used as precipitation agent having been liberated at least partially from lactose before the treatment of exchange of cations;
- The whey used as precipitation agent having been liberated at least partially from albumin before the treatment of exchange of cations;
- The whey used as precipitation agent having been liberated from albumin and from lactose together;

- The whey used as precipitation agent being obtained by diluting the slurry of whey after removal of lactose in view of raising its pH to 4.3 to 4.8, with the aid of a product like sweet whey of cheese or the water after rinsing the lactose, then heating (the diluted whey) to 90 to 95°C, and, after having eliminated the albumin in so doing, treating it in a cation-exchanger.

Surprisingly, by providing casein containing TGF-β2 obtainable by a "mild" process as depicted above, the TGF-β2 is not irreversibly inactivated during processing and will not be inactivated during passage through the acidic environment of the stomach. Remarkably, the casein fraction obtained associates with and protects TGF-β2 and prevents its inactivation until arrival in the small intestine. It is further very surprising that casein with TGFβ2 is obtained, since TGF-β2 is a soluble factor, which is usually found in the whey fraction.

Due to the protective properties of the casein containing TGF-β, the amount of TGF-β to be administered in order to obtain the beneficial effects claimed herein, are be clearly lower as compared to other ways of administering TGF-β, which lack a protective principle.

In a preferred embodiment, of the composition according to the invention, the casein containingTGF-β comprises 0.25 - 5, preferably 0.3 - 2.5, more preferably 1 - 2 μg of active TGF-β per g of casein.

In a preferred embodiment, the composition according to the invention preferably comprises 0.5 – 20, preferably 0.8 – 6.5, most preferably 1.5 – 4 μg of active TGF-β per 100 kcal of the nutritional composition.

Whey proteins may be commercially obtained. Preferably, whey protein with high amounts of bio-active proteins is used. Suppliers of milk products such as whey and further fractions of whey, for example lactoferrin, etc are Arla Foods Ingredients, Morigana Milk Industry Co. Ltd (Japan), Tuna in New Zealand

quantitative ELISA kit is commercially available for bovine TGF-β2, from R&D Systems (Catalogue number, DB250).

For sCD14, the presence can be examined by Western blot using an anti-CD14 antibody (BIG14 of Biometec GmbH).

Presence of GLP-2 may be assessed using the anti-human GLP-2 antibodies of Alpha Diagnostic International Inc. or Biodesign International.

A goat anti-TLR-2 polyclonal antibody from the company Santa Cruz may be used to identify soluble TLR-2 in milk by Western blot.

In a preferred embodiment of the present invention, the protein source further comprises added amino acids selected from the group of branched amino acids, glutamine, arginine, threonine, proline and mixtures of these.

"Added amino acids", in the context of the present invention, refers to amino acids that are not protein-bound, but which are added separately from typical dietetic protein sources, such as milk, meat and vegetable proteins, such as legume-protein. The added amino acids may be present as free amino acids and/or as di- and/or tri-peptides comprising these amino acids. For example, the composition may comprise added amino acids in the form of di-peptides of arginine and/or glutamine.

Branched amino acids may be added to the composition according to the present invention and may be selected from the group of leucine, isoleucine, valine and mixtures of these. Preferably, the composition comprises added leucine and valine.

The sum of added branched amino acids, such as leucine and valine, for example, may provide 0-8%, preferably 1-7%, more preferably 2-5% of the total energy of the composition.

The protein source of the composition may further comprise added amino acids selected from the group of arginine, threonine, proline, or mixtures of these. If one or more of these amino acids are added, each of them preferably provides 0-

8%, more preferably 0.5-6%, most preferably 1-3% of the total energy of the composition.

Preferably, the protein source comprises glutamine in the form of an added amino acid. In an embodiment of the invention, the protein source further comprises added glutamine, which provides 2-15% of the energy of the composition.

Added glutamine may be present in the form of a free amino acid, or in the form of a di- or tripeptide. For example, glutamine may be provided as alanyl-, leucyl-, isoleucyl-, valyl-, arginyl-, or prolyl-glutamine, for example. If the composition is a powdered, reconstitutable composition, glutamine is preferably present in the form of a free amino acid.

Preferably, the protein source comprises 50-85% by weight of milk protein and 15-50% of added glutamine, more preferably, the protein source of the composition comprises 60-75% by weight of milk protein and 25-40% by weight of added glutamine.

In terms of energy provided by the protein source, the protein source of the composition according to the present invention provides 20-30%, preferably, 21-29%, more preferably 22-27% of the energy of the nutritional composition.

Preferably, the milk protein provides 10-22%, preferably 15-20% of the energy of the nutritional composition.

Preferably, added glutamine provides about 2-15%, preferably 4-13%, more preferably 6-10% of the energy of the nutritional composition.

Preferably, the sum of protein-bound and added glutamine provides 7-15%, preferably 8-12% of the energy of the composition.

than Glutamine provides up to 5%, more preferably 1-3% of the energy of the composition.

Other sources of protein further include meat protein, or vegetable protein such as soy, rice, pea, oat protein, and/or mixtures thereof, for example.

The protein source according to the invention may be in the form of intact protein or may be hydrolyzed. Preferably, the protein source comprises intact whey and casein protein.

The nutritional composition according to the present invention comprises a lipid source. Sources of lipids for use in the nutritional composition may be selected from olive oil, sunflower oil, (low erucic) rapeseed oil, hazelnut oil, safflower oil, soy oil, corn oil, coconut oil, milk fat, black currant seed oil, fish oil, palm oil, peanut oil, as well as single cell oils and mixtures of these, for example.

The lipid source may comprise saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), and/or polyunsaturated fatty acids (PUFA). SFA may partially be present as medium chain triglycerides (MCT), MCT referring to triglycerides comprising $C_6 - C_{12}$ fatty acids.

In a preferred embodiment of the present invention, the lipid source comprises, in percent by weight of the lipid source, 30-70%, preferably 40-60%, more preferably 45-55% of MCT.

Preferably, the lipid source provides 25-45%, preferably 30-40%, more preferably, 32-38% of the energy of the composition.

Preferably, the lipid source of the composition comprises n-3 and/or n-6 poly-unsaturated fatty acids (PUFA).

Preferably, the composition according to the invention comprises a n-6/n-3 fatty acid ratio in the range of 2/1 to 8/1, preferably 2/1 to 7/1, more preferably the ratio is in the range of about 2/1 to 5/1.

Preferably, 5-15%, more preferably 8-12%, for example 10% of total fatty acids of the lipid source are present in the form of n-3 fatty acids. Preferably, the n-3 fatty acid is selected from α-linolenic acid (18:3n-3), eicosapentaenoic acid (EPA, 20:5n-3), docosapentaenoic acid (DPA, 22:5n-3), or docosahexaenoic acid (DHA, 22:6n-3) or mixtures of these.

Preferably, n-3 fatty acids are present in an amount, which corresponds to 1-6 g, preferably 2-4 g of n-3 fatty acids per daily intake of the nutritional composition.

Preferably, the composition according to the invention comprises EPA and DHA at a EPA/DHA ratio of 1/1.5 to 1/2.5, for example 1/2. Since molecular weights of EPA and DHA are almost identical, these ratios may be regarded as weight or as molecular ratios.

The composition according the present invention comprises at least one source of digestible carbohydrates. The digestible carbohydrate source may be any suitable carbohydrate or carbohydrate mixtures. For example, the carbohydrate source may be maltodextrin, native or modified starch from tapioca, corn, rice, other cereals, potato, for example, or high amylose starch, sucrose, glucose, fructose, and/or mixtures thereof. Preferably, the digestible carbohydrate source comprises maltodextrin, more preferably maltodextrin and sucrose.

Preferably, the composition according to the present invention is clinically free of lactose. The term "clinically free of lactose" refers, in the context of the present invention, to nutritional compositions that have a maximum of 0.2 g lactose per 100 kcal of the composition. Preferably, the composition has less than 0.2, more preferably less than 0.17 g lactose per 100 kcal of the composition.

The digestible carbohydrate source, may provide 25% to 55% of the energy of the composition; preferably 30% to about 50%, more preferably 35 to 45%, most preferably 37 to 43% of the energy. For example, the carbohydrate source may [illegible]

about 100% to about 250% of the recommended daily allowance of the vitamins and minerals per 1500 calories of the nutritional composition.

Various flavours, sweeteners and other additives may be present.

The composition may further comprise at least one prebiotic. The term prebiotic refers to dietary fibre or other food components that may serve as a substrate for beneficial intestinal bacteria. Preferably, the composition comprises at least one type of soluble fibre, which can serve as a prebiotic.

The prebiotic may be an oligosaccharide or a mixture of different oligo- and/or polysaccharides. Oligosaccharides may be selected from oligosaccharides based on raffinose, galactose, fructose, lactosucrose, xylose, for example. EP 0 307 523 discloses the literature according to which the oligosaccharides may be obtained.

Preferably, the prebiotic is selected from inulin and/or fructooligosaccharides or a combination thereof.

Inulin is a mixture of fructose polymers (F_2-F_{60}), which may be isolated from chicory root by hot water extraction, for example. Inulin, which is obtained in this way is nearly always characterised by a final glucose unit, following the general formula GFn, where n lies between 2-60, preferably between 11-50. Inulin is commercially obtainable from "Orafti", Belgium, under the tradename Raftiline ®, or from Cosucra, under the tradename Frutafit®.

Fructooligasaccharides (FOS) are generally oligopolymers of fructose, which may be obtained in at least two different ways:
(1) hydrolysis of inulin (see above), commercially obtainable from "Orafti", Belgium, under the various different tradenames of Raftilose®.
(2) by synthesis from sucrose with the aid of β-fructofuranosidase from *Aspergillus niger*, commercially obtainable from Meiji Seika Co. of Japan. This latter method does not yield oligosaccharides of more than 5 fructose monosaccharide units (so-called short-chain, SC FOS).

The composition according to the invention preferably comprises a mixture of inulin and FOS, which comprises about 30-80% FOS and 20-70% inulin.

The composition may also comprise other prebiotics, such as further soluble non-starch polysaccharides. For the categorisation of fibre in soluble and insoluble fibre according to solubility in water, the standard protocol is found in L. Prosky et al., J. Assoc. Off. Anal. Chem. 71, 1017-1023 (1988). Examples of typically soluble non-starch polysaccharides are inulin, pectin, β-glucans, various gums such as gum arabic, tragacanth, mucilages, guar and locust bean gum, agar, carageenans, alginates, xanthan and the like. These ingredients are commercially available.

A typical source of soluble fibre is pea inner fibre, also known as pea cellular wall, commercially obtainable from Cosucra under the tradename Sweelite®.

Preferably, the composition comprises, in percent by weight of dry matter, 0-10%, preferably 1-8%, more preferably, 2-5% of a prebiotic.

Preferably, the composition according to the invention comprises one or more probiotics, that is, micro organisms or their fermentation substrate that exert a beneficial effect on the consumer.

Probiotics may be either obtained commercially or they may be produced generally by a fermentation process and, optional, drying. Specific strains often have particular media or substrate preferences, which the skilled person knows about.

The micro-organisms may be in a dried form, or for example in a spore form for micro-organisms which form spores. The drying of micro-organisms after production by fermentation is known to the skilled person. See for example, EP 0 818 529 (SOCIETE DES PRODUITS NESTLE), where a drying process of pulverisation is described, or WO 0144440 (INRA). Usually, bacterial micro-organisms are concentrated from a medium and dried by spray drying. Oil-in-

However, the micro-organisms need not necessarily be present in a dried form. It may also be suitable to mix them directly after fermentation with a powdered nutritional composition, for example, and optionally perform a drying process, preferably at low temperatures (below 70°C) thereafter. Such an approach is disclosed in WO 02065840 (SOCIETE DES PRODUITS NESTLE).

Many probiotics are commercially available and may be obtained in a powdered form various suppliers, for example, *Bifidobacterium lactis* (DSM 20215) may be obtained from Christian Hansen BioSystems A/S (CHL), 10-12 Boge Allé, P.O Box 407, DK-2970 Horsholm, Denmark. Such powders may be directly added (dry-mixed) to powdered nutritional compositions.

The literature mentions some of the micro-organisms from which suitable probiotics may be selected. For example, EP 0 862 863A2, in particular on page 3, lines 25 – 37, comprises a list from which the probiotic according to the present invention may be selected.

For example, the selected probiotic is a *Bifidobacterium*. Preferably, it is a *Bifidobacterium lactis* or a *Bifidobacterium longum*.

For example, the selected probiotic is a *Lactobacillus paracasei*. Preferably, the selected probiotic is selected from the group consisting of *Bifidobacterium longum* (CNCM I-2170), *Bifidobacterium lactis* (German Culture Collection: DSM20215), *Lactobacillus paracasei* (CNCM I-2116, CNCM I-1292), *Lactobacillus johnsonii* (CNCM I-1225) or mixtures thereof.

The term probiotic also includes dead probiotic bacteria, fermentation substrate and/or probiotic-derived material.

For example, the nutritional composition according to the invention may comprise 10^5-10^{11}, more preferably 10^6-10^9 cfu per daily serving of the nutritional composition. If the composition of the invention serves as complete nutrition, the daily serving may be divided up in several servings and corresponds to about 1.5 to 2 L of the nutritional composition of the invention, optionally if reconstituted.

If the composition is powdered, it preferably comprises 10^5-10^{11} cfu per 75 g of the powdered composition.

In a preferred embodiment, the composition according to the present invention has a caloric density of 1.3-1.8 kcal/ml, optionally after reconstitution. Preferably, it has a caloric density of 1.4-1.7, more preferably 1.4-1.6 kcal/ml. The composition is preferably used as a supplement to an individual's diet, however, it may also be designed to provide complete nutritional support.

Preferably, the composition according to the invention is powdered. Accordingly, it may be reconstituted upon addition of water, such as boiled and cooled tap water, or otherwise nutritionally safe water.

Alternatively, the powdered composition may also be reconstituted with juice, such as apple juice, flavoured waters or other beverages. Preferably, these beverages have a neutral pH. In most of these later cases, the composition may not be diluted up to preferred concentration, due to the substantial dry matter content or low pH possibly present in the juice or the other beverage.

Preferably, if the composition is powdered, 50-100g, more preferably 60-90g of the powdered composition are mixed with 230 ml water and shaken or stirred. The composition may be administered orally or tube fed.

When the product is used as exclusive nutrition, preferably, 1.0-2.5, more preferably 1.2-2.0 L, for example 1.5 L of the reconstituted nutritional composition are administered per day.

According to an embodiment of the invention, the composition is used for alleviating and/or reducing side effects of chemotherapy and/or radiotherapy.

For example, the side effects of chemotherapy and/or radiation therapy are one or

In a further embodiment of the present invention, the chemotherapy and/or radiotherapy is applied to treat a cancer patient.

According to a further embodiment, the composition is used for providing nutrition during cancer therapy, preferably, for providing complete nutrition.

In another embodiment, the invention relates to the composition of the invention for treating and/or preventing damages or loss of structure of the small intestine, of the intestinal mucosa, of epithelial intestinal cells and/or mucositis. In particular, the side effect is mucositis.

In still another embodiment, the composition of the invention is used for treating and/or preventing dietary intolerance.

The composition of the present invention may also be used in the preparation of nutritional compositions, medicaments or other forms of orally administered therapy for treating, preventing or alleviating side effects of radiation and chemotherapy.

The nutritional composition according to the invention may be produced as is conventional; for example, by blending together the protein source comprising bio-active milk proteins, and free amino acids, the carbohydrate source, and the lipid source. If used, the emulsifiers may be included in the blend. The vitamins and minerals may be added at this point but may also be added later to avoid thermal degradation. Any lipophilic vitamins, emulsifiers and the like may be dissolved into the lipid source prior to blending. Water, preferably water, which has been subjected to reverse osmosis, may then be mixed in to form a liquid mixture. The temperature of the water is conveniently about 50°C to about 80°C to aid dispersal of the ingredients. Commercially available liquefiers may be used to form the liquid mixture.

The liquid mixture may then be thermally treated to reduce bacterial loads. For example, the liquid mixture may be rapidly heated to a temperature in the range of about 80°C to about 110°C for about 5 seconds to about 5 minutes. This may be carried out by steam injection or by heat exchanger; for example a plate heat exchanger.

The liquid mixture may then be cooled to about 60°C to about 85°C; for example by flash cooling. The liquid mixture is then homogenised. The homogenised mixture may then be further cooled to add any heat sensitive components; such as vitamins and minerals. The pH and solids content of the homogenised mixture is conveniently standardised at this point.

The mixture is evaporated and dried to powder; for example by spray drying. Conventional procedures may be used.

Probiotics and further heat sensitive ingredients, if not added before drying, such as certain minerals may now be added to the dried composition.

Example 1

A powdered nutritional composition is prepared with the ingredients given in **Table 1** below.

Ingredient	g / 100 g of dried components	Energy (1.5 kcal per ml)
Protein source (total): Casein Whey Glutamine	30 12.2 8.2 9.6	25% 10.2% 6.8% 8%
Lipid source (total): MCT (Coconut oil) Other lipids n-6/n-3 ratio	18.4 9.2 9.2 2/1	35%
Carbohydrates (total): Maltodextrin	47.4	40%
Vitamins and minerals are added according to daily requirements		

include the technical terms dispersion or suspension). The solution is standardised to a total solids content (TS) of 25%. Hydration time is adapted to have a good hydration of the protein.

Vitamins and minerals are added to the solution.

The pH is adjusted with KOH or citric acid to a value between 6.8-7.

The solution is pre-heated to 50°C, as well as the lipid source comprising MCT (Medium Chain triglicerides), low eruic rapeseed oil, and corn oil. The lipid source is then added in-line, that is, directly in the tube with the flowing product.

The solution, including the added lipid source, is heated to 105°C by direct steam injection by a steam injection valve and the temperature held for 5 seconds.

Then the product is directly flashed into an evaporator, in which the product is concentrated up to 40-50% total solids (dry matter) by a Scheffers falling-film evaporator.

Thereafter, the concentrated solution is conducted to a buffer tank for homogenisation, where it is pre-heated to 75°C, homogenised at 150 bars with a high pressure pump and then spray dried.

The powdered solution is then supplied with Soya Lecithin and maybe then supplied with vitamin premix, mineral premix or prebiotics and a small part of the maltodextrin.

Then the powder maybe filled into gassed cans or gassed pouches. The gas is composed by N_2 and CO_2

The powder obtained is a nutritional composition particularly suitable as complete nutrition for patients undergoing anti-cancer treatments. The powder may be reconstituted with tap water. The recommended daily serving size for an adult patient would be 152 g powder per day.

Claims

1. A nutritional composition comprising a protein, a lipid and a carbohydrate source, which provides, in its liquid state, at least 1.3 kcal per ml, and which is characterised in that the protein source provides 20-30% of the energy of the composition and comprises milk protein containing bio-active proteins.

2. The composition according to Claim 1, wherein the milk protein comprises, 40-80% by weight of casein and 60-20% whey.

3. The composition according to Claim 1, wherein the milk protein comprises casein containing TGF-β.

4. The composition according to Claim 1, which comprises 0.5 – 20 μg of TGF-β per 100 kcal of the nutritional composition.

5. The composition according to Claim 1, wherein the protein source further comprises added amino acids selected from the group of branched amino acids, glutamine, arginine, threonine, proline and mixtures of these.

6. The composition according to Claim 1, wherein the protein source further comprises added glutamine, which provides 2-15% of the energy of the composition.

7. The composition according to claim 1, which comprises whey or casein containing soluble CD14, Glucagon-like peptide 2, soluble Toll-2 receptor or a mixture containing several or all of these.

8. The composition according to Claim 1, which has a caloric density of 1.2-2 kcal/ml, optionally after reconstitution.

[illegible]

10. The composition according to claim 1 for alleviating and/or reducing side effects of chemotherapy and/or radiotherapy.

11. The composition according to Claim 1, wherein the chemotherapy and/or radiotherapy is applied to treat a cancer patient.

12. The composition according to claim 10, wherein the side effects of chemotherapy and/or radiation therapy are one or several of diarrhoea, stomatitis, infections, increased intestinal permeability, lack of absorption, leukopenia, endotoxemia, the acute phase reponse, or the presence of hepatic enzymes in the serum.

13. The composition according to Claim 1 for providing nutrition during cancer therapy.

14. The composition according to Claim 1 for treating and/or preventing dietary intolerance.

15. Method for preventing, treating or alleviating side-effects during chemotherapy and/or radiation therapy comprising the step of administering the nutritional composition according to Claim 1.

Abstract

Nutritional Composition against Side Effects of Chemotherapy or Radiotherapy

The present invention relates to a nutritional composition suitable for patients undergoing chemotherapy and/or radiation such as cancer patients. The composition, which is preferably powdered, comprises milk protein containing bioactive factors such as, in a preferred embodiment, added glutamine in the form of a free amino acid.

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